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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,752	10/30/2001	Ramy Lidor-Hadas	1662/55002	8981

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EXAMINER

OH, TAYLOR V

ART UNIT

PAPER NUMBER

1625

DATE MAILED: 01/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/016,752

Applicant(s)

LIDOR-HADAS ET AL.

Examiner

Taylor Victor Oh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 October 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-93 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-93 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 October 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 and 6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Claims 18 and 72 are objected to because of the following informalities: terms “ondansetron hydrochloride methanolate” and “sonication” are written. However, Appropriate spelling correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 9, 19-23, 39-45, 49-50, 52, 57-58, 62-67, 71, and 87-91 are rejected under 35 U.S.C. 102(b) as being anticipated clearly by Wu Gousheng et al (CN 1113234).

Wu Gousheng et al discloses a 1,1,2,2,3-pentahydrogen-9-methyl-3(2'-methyl-imidazole-1)-methyl)-4-oxocarbazole hydrochloride monohydrate compound (see page 16 on its translation, lines 20-22); furthermore, an organic base and standard physiological salt and solvate can be incorporated into the compound in order to be used as a medication for treating nausea and vomiting (see abstract). Moreover, concerning X-ray diffraction patterns and the range of particle size, they are inherently present in the compound and also naturally obtained as unique characteristics for evaluating the compound, not as the novelty of the invention. This compound is identical with the claims.

Claim Rejections - 35 USC § 103

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 5-8, 10-18, 24-38, 46-48, 51, 53-56, 59-61, 68-70 77-86, 92 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wu Gousheng et al (CN 1113234).

Wu Gousheng et al discloses a 1,1,2,2,3-pentahydrogen-9-methyl-3(2'-methyl-imidazole-1)-methyl)-4-oxocarbazole hydrochloride monohydrate compound (see page 16 on its translation, lines 20-22); furthermore, an organic base and standard physiological salt and solvate

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can be incorporated into the compound in order to be used as a medication for treating nausea and vomiting (see abstract). Concerning the production of the 1,1,2,2,3-pentahydrogen-9-methyl-3((2'-methyl-imidazole-1)-methyl)-4-oxocarbazole hydrochloride dihydrate compound, the following steps can be used:

1. dissolving the compound of 1,1,2,2,3-pentahydrogen-9-methyl-3((2'-methyl-imidazole-1)-methyl)-4-oxocarbazole in 5 ml of ethanol;
2. blowing dry HCl into the solution;
3. cooling down the resultant mixture, crystallizing the compound , and recrystallizing it with water , thereby obtaining the 1,1,2,2,3-pentahydrogen-9-methyl-3((2'-methyl-imidazole-1)-methyl)-4-oxocarbazole hydrochloride dihydrate compound (see page 21 , lines 8-17).

Furthermore, in order to isolate the 1,1,2,2,3- pentahydrogen-9-methyl-3((2'-methyl-imidazole-1)-methyl)-4-oxocarbazole hydrochloride monohydrate compound, the 1,1,2,2,3-pentahydrogen-9-methyl-3((2'-methyl-imidazole-1)-methyl)-4-oxocarbazole hydrochloride dihydrate compound is recrystallized with water and dried in a drier containing P_2O_5 (see page 17 , lines 16-17).

Moreover, there is a general procedure for producing the 1,1,2,2,3-pentahydrogen-9-methyl-3((2'-methyl-imidazole-1)-methyl)-4-oxocarbazole hydrochloride with an aqueous solvent by dissolving the 1,1,2,2,3- pentahydrogen-9-methyl-3((2'-methyl-imidazole-1)-methyl)-4-oxocarbazole to a water /alcohol solvent and adding hydrogen chloride (1N) to the resultant mixture to produce the desired compound (see page 8 , lines 19-24).

However, Wu Gousheng et al differs from the instant invention in that a solvent system contains chloroform, toluene, ketone, xylene, isopropanol, methyl tert-butyl ether during the process; the exposure is for a period of three weeks or less or 30 to 70 hours; the temperature is from -15°C to room temperature; and the mechanical agitation is sonification.

Concerning the use of the various solvent system for producing the desired compound, the reference is silent about them. However, the Wu Gousheng et al does indicate the use of benzene and n-propanol, which are similar to the functionality of the claimed solvents. Therefore, there is no patentable weight over the prior art reference in the absence of an unexpected result using the claimed solvent system.

With respect to the exposing period of three weeks or less or 30 to 70 hours and the temperature is from -15°C to room temperature, the limitation of a process with respect to ranges of pH, time and temperature does not impart patentability to a process when such values are those which would be determined by one of ordinary skill in the art in achieving optimum operation of the process. Temperature and period are well understood by those of ordinary skill in the art to be a result-effective variable, especially when attempting to control selectivity of a chemical process.

Regarding the use of the mechanical agitation by a sonic vibration, this is directly related to mechanical expediency. Therefore, it would have been obvious to the skilled artisan in the art to have motivated to employ the sonic vibration as mechanical expediency in order to accelerate the process.

Wu Gousheng et al does teach the general procedure for producing the 1,1,2,2,3-pentahydrogen-9-methyl-3((2'-methyl-imidazole-1)-methyl)-4-oxocarbazole hydrochloride with an aqueous solvent by dissolving the 1,1,2,2,3- pentahydrogen-9-methyl-3((2'-methyl-imidazole-1)-methyl)-4-oxocarbazole to a water /alcohol solvent and adding hydrogen chloride (1N) to the resultant mixture to produce the desired compound. Furthermore, in order to optimize the reaction conditions such as time and temperature for the process, it would have been obvious to the skilled artisan in the art to have motivated to modify the period and temperature to the claimed parameters by routine experimentation, thereby accelerating the reaction process.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Coates et al (U.S. 4,749,718) teaches carbazole derivatives and their use as 5HT-induced antagonists. They are useful in the treatment of psychotic disorders, nausea, and vomiting. Suitable physiologically acceptable salts of the compounds of general formula include hydrochlorides; furthermore, hydrates can be used as their solvates.

Collin (U.S. 5,344,658) teaches a process for reducing the crystal size of ondansetron hydrochloride dihydrate produced by crystallization from a solvent system; the ondansetron hydrochloride dihydrate is desolvated by drying at an elevated temperature and reduced pressure and is then rehydrated.

Coates et al (U.S. 4,859,662) teaches tetrahydro-imidazolymethyl-carbazolones and their analogs for treating 5HT function disturbances. They are useful in the treatment of psychotic

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disorders, nausea, and vomiting. Suitable physiologically acceptable salts of the compounds of general formula include hydrochlorides; furthermore, hydrates can be used as their solvates.

Collin (U.S. 5,622,720) teaches a process for reducing the crystal size of ondansetron hydrochloride dihydrate produced by crystallization from a solvent system in which the ondansetron hydrochloride dihydrate is desolvated by drying at an elevated temperature and reduced pressure and is then rehydrated. Furthermore, the resultant crystals are suitable for homogeneous distribution in a tablet blend in order to treat nausea, and vomiting.

Bell et al (GB 2,153,821) teaches 3-imidazolymethyl-1,2,3,9-tetrahydro-4H-carbazol-4-one derivatives and their use as 5HT-induced antagonists. They are useful in the treatment of psychotic disorders such as schizophrenia, nausea, and vomiting. Suitable physiologically acceptable salts of the compounds of general formula include hydrochlorides; furthermore, hydrates can be used as their solvates.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 703-305-0809. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman can be reached on 703-308-4698. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-2742 for regular communications and 703-305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

rv
12/4/02

Alan L Rotman
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